

REMARKS/ARGUMENTS

The Status of the Claims.

Claims 1-25 are pending. Claims 8-25 were withdrawn from current consideration pursuant to a restriction requirement. Claims 1, 4, 5, 6, 7 and 8 were previously amended.

35 U.S.C. §103(a).

Claims 1-7 were rejected under 35 U.S.C. §103(a) as allegedly obvious over a combination three or more references, including: Pliml et al., Clinical Investigator, 71 (10):770-73 (1993); Stanley et al. Cardiovascular Research, 33:243-257 (1997); PCT publication WO 98/11435 to Hoeft Rademacher Ltd; and US patent 4,880,783 to Mentzer. Applicants traverse.

The Office Action points out that Pliml mentions ribose can be used to treat ischemic heart disease. The Examiner further alleges that Stanley teaches that one potential method of treating heart disease is by directly activating PDH. Finally, Rademacher (WO 98/ 11435) is alleged to teach that IPG P-type activates pyruvate dehydrogenase phosphatase, and can be employed as a therapeutic agent for the treatment of diabetes. This mix of technologies is combined to suggest that it would be obvious to combine ribose with IPGs as a treatment for ischaemia to achieve the invention of claims 1-7. However, such a combination is unmotivated, fails to provide an obvious combination under *In re Kerkhoven*, 205 U.S.P.Q. 1069, and would employ different principles of operation than the cited references.

Three requirements must be met for a *prima facie* case of obviousness. First, the prior art reference must teach all of the limitations of the claims. M.P.E.P. § 2143.03. Second, there must be a motivation to modify the reference or combine the teachings to produce the claimed invention. M.P.E.P. § 2143.01. *In re Geiger*, 815 USPQ2s 1276, 1278 (Fed. Cir. 1987). Third, a reasonable expectation of success is required. M.P.E.P. § 2143.02. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 5 USPQ2d

1529, 1531 (Fed. Cir. 1988). Both the motivation to combine and the expectation of success must be found in the prior art, and not based on Applicants' disclosure. M.P.E.P. §2143.

The combination between each of the three references lacks motivation to make an appropriate modification in each case. No motivation exists in any of the references or the art to make such a combination. Stanley mentions theoretical PDH activation therapies, but provides no specifics and concludes with the statement that "[i]t is not yet clear which of these approaches offers the best treatment of cardiac ischaemia". Stanley does not mention ribose or IPGs in any composition. Rademacher states that his work suggests "that an inappropriately low IPG P-type might be associated with a diminished activity of PDH phosphatase...", (emphasis added). Rademacher is concerned with the treatment of diabetes, and thus fails logically to motivate combination of IPG with ribose (a drug treating reperfusion disease). Pliml mentions that ribose has been used in treatment of ischemic heart disease and muscular enzyme deficiencies but focuses on a study of ribose toxicity without suggesting combination therapeutic compositions. The cited art is lacking motivation to provide each of the several associations necessary to allegedly provide, e.g., the composition of claim 1. The motivation provided in rejection of the claims, that one skilled in the art would have been motivated, is insufficient. Merely stating that the claimed invention is within the capabilities of one skilled in the art (OSA) does not state a case of obviousness, see *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000).

The Examiner cites *In re Kerkhoven*, to argue that "it is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose." However, application of this rule to the facts of the present application leads to the conclusion of nonobviousness on multiple grounds. Firstly, the cited references do not teach ribose and IPG as having the same utility. Secondly, any new composition based on mixture of the cited compositions would not form a composition useful for the very same purpose taught by the cited references, as required by *Kerkhoven*. Whereas Rademacher teaches IGP-P might affect the activity of PDH phosphatase in treatment of diabetes, Pliml fails to offer a mechanism for the suggestion ribose can treat some

undisclosed aspect of ischemic heart disease - different utilities for different purposes. The obviousness rejections should be withdrawn according to Kerkhoven analysis.

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. In *re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). The compositions of the invention can provide different and complimentary activities (see the specification and previous response) for qualitatively improved treatment results over, e.g., ribose or IPG treatments alone. The principle of operation of the present composition is different from that of the separate components. For example, coadministration of a mitochondrial oxidative phosphorylation stimulator (e.g., IPG), changes the benefit from administration of ribose by providing two distinct means of replenishing the energy charge of the cell, and so increasing the rate at which regenerative pathways can operate. In addition, use of IPGs to activate PDH enables ATP to be synthesized following ischaemia without production of lactic acid. Such ATP can be useful in the processing of ribose in recovery from ischemia. Thus, as explained in the teachings of the present application, the present invention provides unexpectedly different superior results with respect to the prior art, indicating that the invention is not obvious.

As claim 1 is not obvious in light of the cited references, Applicant requests the rejection based on obviousness be withdrawn. Furthermore, because all the remaining claims under consideration are dependent on claim 1, they too are nonobvious and rejections should be withdrawn.

With regard to the rejection of claim 4, as a claim dependent on nonobvious claim 1, is can not be obvious. Furthermore, to allegedly provide all the limitations of claim 4, the Examiner has offered the Mentzer reference, bringing the total references in the allegedly obvious combination to four. The motivation, Kerkhoven analyses, and changed principles arguments favor the present invention all the more with this additional citation. Mentzer does not provide a motivation for the combination of claim 4. The mechanisms and purpose of Mentzer compositions are not the same as the other composition references. Applicant respectfully requests the obviousness rejection of claim 4 be withdrawn.

Appl. No. 09/719,909
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Reply to Office action of April 22, 2004

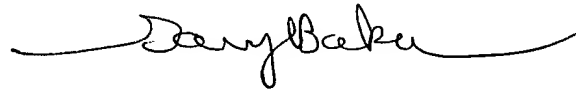
CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Response, a telephone interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 769-3510 to schedule an interview.

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Respectfully submitted,



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Attachments:

- 1) A petition to extend the period of response for 1 month;
- 2) A transmittal sheet;
- 3) A fee transmittal sheet;
- 4) A receipt indication postcard.

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